Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

	Application Number		10552194
INFORMATION BIOCH COURT	Filing Date		2006-10-12
INFORMATION DISCLOSURE	First Named Inventor	med Inventor Matthew Nugent	
STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Art Unit		1651
( NOTION SUBMISSION UNICE STOLEN 1.33)	Examiner Name	Thane	e E UNDERDAHL
	Attorney Docket Numb	er	701586-053702

					U.S.I	PATENTS			Remove		
Examiner Initial*	Cite No	Patent Number	Kind Code <sup>1</sup>	Issue D	)ate	Name of Pate of cited Docu	entee or Applicant ment	Releva		ines where	
	1										
If you wis	h to a	⊥ dd additional U.S. Pater	ıt citatio	n inform	ation pl	ease click the	Add button.		Add		
			U.S.P	ATENT	APPLIC	CATION PUBI	LICATIONS		Remove		
Examiner Initial*	Cite No	Publication Number	Kind Code <sup>1</sup>	Publica Date	ition	Name of Pate of cited Docu	entee or Applicant ment	Releva		ines where es or Relev	
	1										
If you wis	n to a	dd additional U.S. Publi	shed Ap	plication	r citation	n information p	olease click the Add	d button			
				FOREIG	ON PAT	ENT DOCUM	ENTS		Remove		
Examiner Initial*	Cite No	Foreign Document Number <sup>3</sup>	Country Code <sup>2</sup>		Kind Code <sup>4</sup>	Publication Date	Name of Patentee Applicant of cited Document	e or V F	vhere Rele	or Relevant	T5
	1										
If you wis	n to a	। dd additional Foreign Pa	atent Do	cument	ı citation	information pl	⊥ lease click the Add	button	Add		
			NON	I-PATE	NT LITE	RATURE DO	CUMENTS		Remove		
Examiner Initials*											

Application Number		10552194		
Filing Date		2006-10-12		
First Named Inventor Matth		ew Nugent		
Art Unit		1651		
Examiner Name Thane		E UNDERDAHL		
Attorney Docket Number		701586-053702		

1	Risau, W., "Mechanisms of angiogenesis." (1997) Nature 386, 671-674.	
2	Veikkola, T., Karkkainen, M., Claesson-Welsh, L., and Alitalo, K., "Regulation of Angiogenesis via Vascular Endothelial Growth Factor Receptors." (2000) Cancer Res 60, 203-212.	
3	Robinson, C. J., and Stringer, S. E., "The splice variants of vascular endothelial growth factor (VEGF) and their receptors." (2001) J Cell Sci 114, 853-865.	
4	Park, J. E., Keller, G. A., and Ferrara, N., "The Vascular Endothelial Growth Factor (VEGF) Isoforms: Differential Deposition into the Subepithelial Extracellular Matrix and Bioactivity of Extracellular Matrix-bound VEGF." (1993) Mol Biol Cell 4, 1317-1326.	
5	Bernfield, M., Gotte, M., Park, P. W., Reizes, O., Fitzgerald, M. L., Lincecum, J., and Zako, M., "Functions of Cell Surface Heparan Sulfate Proteoglycans." (1999) Annu Rev Biochem 68, 729-777.	
6	Woods, A., Oh, E. S., and Couchman, J. R., "Syndecan Proteoglycans and Cell Adhesion." (1998) Matrix Biol 17, 477-483.	
7	Park, P. W., Reizes, O., and Bernfield, M., "Cell Surface Heparan Sulfate Proteoglycans: Selective Regulators of Ligand-Receptor Encounters." (2000) J Biol Chem 275, 29923-29926.	
8	Turnbull, J., Powell, A., and Guimond, S., "Heparan sulfate: decoding a dynamic multifunctional cell regulator." (2001) Trends Cell Biol 11, 75-82.	
9	Esko, J. D., and Lindahl, U., "Molecular diversity of heparan sulfate." (2001) J Clin Invest 108, 169-173.	
10	Nugent, M. A., and Iozzo, R. V., "Fibroblast growth factor-2." (2000) Int J Biochem Cell Biol 32, 115-120.	
11	Rapraeger, A. C., Krufka, A., and Olwin, B. B., "Requirement of Heparan Sulfate for bFGF-Mediated Fibroblast Growth and Myoblast Differentiation." (1991) Science 252, 1705-1708.	

Application Number		10552194		
Filing Date		2006-10-12		
First Named Inventor Matth		ew Nugent		
Art Unit		1651		
Examiner Name Thane		E UNDERDAHL		
Attorney Docket Number		701586-053702		

Fannon, M., Forsten, K. E., and Nugent, M. A., "Potentiation and Inhibition of bFGF Binding by Heparin: A Model for Regulation of Cellular Response." (2000) Blochemistry 39, 1434-1445.    13   Gitay-Goren, H., Soker, S., Wodavsky, I., and Neufeld, G., "The Binding of Vascular Endothelial Growth Factor to Its Receptors is Dependent on Cell Surface-associated Heparin-like Molecules." (1992) J Biol Chem 267, 6083-6098.       14   Tessler, S., Rockwell, P., Hicklin, D., Cohen, T., Levi, B. Z., Witte, L., Lemischka, I. R., and Neufeld, G., "Heparin Modulates the Interaction of VEGF165 with Soluble and Cell Associated filk-1 Receptors." (1994) J Biol Chem 269, 12456-12461.       15   Gengrinovitch, S., Berman, B., David, G., Witte, L., Neufeld, G., and Ron, D., "Glyploan-1 Is a VEGF165 Binding Proteoglycan That Acts as an Extracellular Chaperone for VEGF165* (1999) J Biol Chem 274, 10816-10822.       16   Iozzo, R. V., and San Antonio, J. D., "Heparan sulfate proteoglycans: heavy hitters in the angiogenesis arena." (2001)       17   Sharma, B., Handler, M., Eichstetter, I., Whitelook, J. M., Nugent, M. A., and Iozzo, R. V., "Antisense Targeting of Perlecan Blocks Tumor Growth and Angiogenesis in Vivo" (1998) J Clin Invest 102, 1593-1608       18   Kleeff, J., Ishiwata, T., Kumbasar, A., Friess, H., Buchler, M. W., Lander, A. D., and Korc, M., The Cell-surface Heparan Sulfate Proteoglycan Glypican-1 Regulates Growth Factor Action in Pancreatic Carcinoma Cells and Is Overexpressed in Human Pancreatic Cancer." (1998) J Clin Invest 102, 1662-1673.       19   Folkman, J., "Angiogenesis in cancer, vascular, rheumatoid and other disease." (1995) Nat Med 1, 27-31.       20   Tannock, I. F., "Oxygen diffusion and the distribution of cellular radiosensitivity in tumours." (1972) Br J Radiol 45, 1515-524.       21   Shweiki, D., Neeman, M., Itin, A., and Keshelt, E., "Induction of vascular endothelial growth factor expression by hypoxia and by glucose defliciency in multicell spheroids: Implications for tumor angiogenesis." (19			
Tessler, S., Rockwell, P., Hicklin, D., Cohen, T., Levi, B. Z., Witte, L., Lemischka, L. R., and Neufeld, G., "Heparin Modulates the Interaction of VEGF165 with Soluble and Cell Associated fik-1 Receptors." (1994) J Biol Chem 269, 12456-12461.  [15] Gengrinovitch, S., Berman, B., David, G., Witte, L., Neufeld, G., and Ron, D., "Glypican-1 Is a VEGF165 Binding Profeoglycan That Acts as an Extracellular Chaperone for VEGF165." (1999) J Biol Chem 274, 10816-10822.  [16] Lozzo, R. V., and San Antonio, J. D., "Heparan sulfate profeoglycans: heavy hitters in the ang ogenesis arena." (2001) J Clin Invest 108, 349-355.  [17] Sharma, B., Handler, M., Eichstetter, I., Whitelock, J. M., Nugent, M. A., and Iozzo, R. V., "Antisense Targeting of Perfecan Blocks Tumor Growth and Angiogenesis In Vivo." (1998) J Clin Invest 102, 1599-1608.  [18] Kleeff, J., Ishiwata, T., Kumbasar, A., Friess, H., Buchler, M. W., Lander, A. D., and Korc, M., "The Cell-surface Heparan Sulfate Profeoglycan Glypican-1 Regulates Growth Factor Action in Pancreatic Carcinoma Cells and Is Overexpressed in Human Pancreatic Cancer." (1998) J Clin Invest 102, 1662-1673.  [19] Folkman, J., "Angiogenesis in cancer, vascular, rheumatoid and other disease." (1995) Nat Med 1, 27-31.  [20] Tannock, I. F., "Oxygen diffusion and the distribution of cellular rad osensitivity in tumours." (1972) Br J Radiol 45, 515-524.  [21] Shweiki, D., Neeman, M., Itin, A., and Keshet, E., "Induction of vascular endothelial growth factor expression by hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad Sci U S A 92, 768-772.	12		
14   Modulates the Interaction of VEGF165 with Soluble and Cell Associated flk-1 Receptors." (1994) J Biol Chem 269,   12456-12461.	13		
Proteoglycan That Acts as an Extracellular Chaperone for VEGF165." (1999) J Biol Chem 274, 10816-10822.	14	Modulates the Interaction of VEGF165 with Soluble and Cell Associated flk-1 Receptors." (1994) J Biol Chem 269,	
J Clin Invest 108, 349-355.  Sharma, B., Handler, M., Eichstetter, I., Whitelock, J. M., Nugent, M. A., and lozzo, R. V., "Antisense Targeting of Perlecan Blocks Tumor Growth and Angiogenesis In Vivo." (1998) J Clin Invest 102, 1599-1608.  Kleeff, J., Ishiwata, T., Kumbasar, A., Friess, H., Buchler, M. W., Lander, A. D., and Korc, M., "The Cell-surface Heparan Sulfate Proteoglycan Glypican-1 Regulates Growth Factor Action in Pancreatic Carcinoma Cells and Is Overexpressed in Human Pancreatic Cancer." (1998) J Clin Invest 102, 1662-1673.  Polkman, J., "Angiogenesis in cancer, vascular, rheumatoid and other disease." (1995) Nat Med 1, 27-31.  Tannock, I. F., "Oxygen diffusion and the distribution of cellular radiosensitivity in tumours." (1972) Br J Radiol 45, 515-524.  Shweiki, D., Neeman, M., Itin, A., and Keshet, E., "Induction of vascular endothelial growth factor expression by hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad Sci U S A 92, 768-772.	15		
Perlecan Blocks Tumor Growth and Angiogenesis In Vivo." (1998) J Clin Invest 102, 1599-1608.	16		
Heparan Sulfate Proteoglycan Glypican-1 Regulates Growth Factor Action in Pancreatic Carcinoma Cells and Is Overexpressed in Human Pancreatic Cancer." (1998) J Clin Invest 102, 1662-1673.  Folkman, J., "Angiogenesis in cancer, vascular, rheumatoid and other disease." (1995) Nat Med 1, 27-31.  Tannock, I. F., "Oxygen diffusion and the distribution of cellular radiosensitivity in tumours." (1972) Br J Radiol 45, 515-524.  Shweiki, D., Neeman, M., Itin, A., and Keshet, E., "Induction of vascular endothelial growth factor expression by hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad Sci U S A 92, 768-772.  Brogi, E., Schatteman, G., Wu, T., Kim, E. A., Varticovski, L., Keyt, B., and Isner, J. M., "Hypoxia-induced Paracrine	17		
Tannock, I. F., "Oxygen diffusion and the distribution of cellular radiosensitivity in tumours." (1972) Br J Radiol 45, 515-524.  Shweiki, D., Neeman, M., Itin, A., and Keshet, E., "Induction of vascular endothelial growth factor expression by hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad Sci U S A 92, 768-772.  Brogi, E., Schatteman, G., Wu, T., Kim, E. A., Varticovski, L., Keyt, B., and Isner, J. M., "Hypoxia-induced Paracrine	18	Heparan Sulfate Proteoglycan Glypican-1 Regulates Growth Factor Action in Pancreatic Carcinoma Cells and Is	
Shweiki, D., Neeman, M., Itin, A., and Keshet, E., "Induction of vascular endothelial growth factor expression by hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad Sci U S A 92, 768-772.  Brogi, E., Schatteman, G., Wu, T., Kim, E. A., Varticovski, L., Keyt, B., and Isner, J. M., "Hypoxia-induced Paracrine	19	Folkman, J., "Angiogenesis in cancer, vascular, rheumatoid and other disease." (1995) Nat Med 1, 27-31.	
21 hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad Sci U S A 92, 768-772.  Brogi, E., Schatteman, G., Wu, T., Kim, E. A., Varticovski, L., Keyt, B., and Isner, J. M., "Hypoxia-induced Paracrine	20		
	21	hypoxia and by glucose deficiency in multicell spheroids: Implications for tumor angiogenesis." (1995) Proc Natl Acad	
	22		

Application Number		10552194		
Filing Date		2006-10-12		
First Named Inventor Matthe		ew Nugent		
Art Unit		1651		
Examiner Name Thane		E UNDERDAHL		
Attorney Docket Number		701586-053702		

23	Gerber, H. P., Condorelli, F., Park, J., and Ferrara, N., "Differential Transcriptional Regulation of the Two Vascular Endothelial Growth Factor Receptor Genes." (1997) J Biol Chem 272, 23659-23667.	
24	Akimoto, T., Liapis, H., and Hammerman, M. R., "Microvessel formation from mouse embryonic aortic explants is oxygen and VEGF dependent." (2002) Am J Physiol Regul Integr Comp Physiol 283, R487-495.	
25	Xu, L., Fukumura, D., and Jain, R. K., "Acidic Extracellular pH Induces Vascular Endothelial Growth Factor (VEGF) in Human Glioblastoma Cells via ERK1/2 MAPK Signaling Pathway." (2002) J Biol Chem 277, 11368-11374.	
26	Nackaerts, K., Verbeken, E., Deneffe, G., Vanderschueren, B., Demedts, M., and David, G., "Heparan Sulfate Proteoglycan Expression in Human Lung-Cancer Cells." (1997) Int J Cancer 74, 335-345.	
27	Matsuda, K., Maruyama, H., Guo, F., Kleeff, J., Itakura, J., Matsumoto, Y., Lander, A. D., and Korc, M., "Glypican-1 Is Overexpressed in Human Breast Cancer and Modulates the Mitogenic Effects of Multiple Heparin-binding Growth Factors in Breast Cancer Cells." (2001) Cancer Res 61, 5562-5569.	
28	D'Arcangelo, D., Facchiano, F., Barlucchi, L. M., Melillo, G., Illi, B., Testolin, L., Gaetano, C., and Capogrossi, M. C., "Acidosis Inhibits Endothelial Cell Apoptosis and Function and Induces Basic Fibroblast Growth Factor and Vascular Endothelial Growth Factor Expression." (2000) Circ Res 86, 312-318.	
29	Nugent, M. A., and Edelman, E. R., "Kinetics of Basic Fibroblast Growth Factor Binding to Its Receptor and Heparan Sulfate Proteoglycan: A Mechanism for Cooperativity." (1992) Biochemistry 31, 8876-8883.	
30	Moscatelli, D., "Metabolism of Receptor-bound and Matrix-bound Basic Fibroblast Growth Factor by Bovine Capillary Endothelial Cells." (1988) J Cell Biol 107, 753-759.	
31	Keyt, B. A., Berleau, L. T., Nguyen, H. V., Chen, H., Heinsohn, H., Vandlen, R., and Ferrara, N., "The Carboxylterminal Domain (111-165) of Vascular Endothelial Growth Factor Is Critical for Its Mitogenic Potency." (1996) J Biol Chem 271, 7788-7795.	
32	Vlodavsky, I., Folkman, J., Sullivan, R., Fridman, R., Ishai-Michaeli, R., Sasse, J., and Klagsbrun, M., "Endothelial cell-derived basic fibroblast growth factor: Synthesis and deposition into subendothelial extracellular matrix." (1987) Proc Natl Acad Sci U S A 84, 2292-2296.	
33	Bashkin, P., Doctrow, S., Klagsbrun, M., Svahn, C. M., Folkman, J., and Vlodavsky, I., "Basic Fibroblast Growth Factor Binds to Subendothelial Extracellular Matrix and Is Released by Heparitinase and Heparin-like Molecules." (1989) Biochemistry 28, 1737-1743.	

Application Number		10552194		
Filing Date		2006-10-12		
First Named Inventor Matthe		ew Nugent		
Art Unit		1651		
Examiner Name Thane		E UNDERDAHL		
Attorney Docket Number		701586-053702		

	34	endothelial growth	man, I., Martial, J., and factor and basic fibrob tor 16-kDa N-terminal f	last growth factor in	capillary e	ndothelial cells is inhib	ited by the	
	35	Forsten, K. E., Akers, R. M., and San Antonio, J. D., "Insulin-Like Growth Factor (IGF) Binding Protein-3 Regulation of IGF-I Is Altered in an Acidic Extracellular Environment." (2001) J Cell Physiol 189, 356-365.						
	36	Wahl, M. L., and Grant, D. S., "Effects of microenvironmental extracellular pH and extracellular matrix proteins on angiostatin's activity and on intracellular pH." (2000) Gen Pharmacol 35, 277-285.						
	37	Detmar, M., Brown, L. F., Berse, B., Jackman, R. W., Elicker, B. M., Dvorak, H. F., and Claffey, K. P., "Hypoxia Regulates the Expression of Vascular Permeability Factor/Vascular Endothelial Growth Factor (VPF/VEGF) and its Receptors in Human Skin." (1997) J Invest Dermatol 108, 263-268.						
	38	Roskams, T., De Vos, R., David, G., Van Damme, B., and Desmet, V., "Heparan Sulphate Proteoglycan Expression in Human Primary Liver Tumours." (1998) J Pathol 185, 290-297.						
	39	Dowd, C. J., Cooney, C. L., and Nugent, M. A., "Heparan Sulfate Mediates bFGF Transport through Basement Membrane by Diffusion with Rapid Reversible Binding." (1999) J Biol Chem 274, 5236-5244.						
	loachim, E., Charchanti, A., Briasoulis, E., Karavasilis, V., Tsanou, H., Arvanitis, D. L., Agnantis, N. J., and Pavlidis, N., "Immunohistochemical expression of extracellular matrix components tenascin, fibronectin, collagen type IV and laminin in breast cancer: their prognostic value and role in tumour invasion and progression." (2002) Eur J Cancer 38, 2362-2370.							
	41	Fairbrother, W. J., Champe, M. A., Christinger, H. W., Keyt, B. A., and Starovasnik, M. A., "Solution structure of the heparin-binding domain of vascular endothelial growth factor." (1998) Structure 6, 637-648.						
Tuder, R. M., Flook, B. E., and Voelkel, N. F., "Increased Gene Expression for VEGF and the VEGF Receptors KDR/Flk and Flt in Lungs Exposed to Acute or to Chronic Hypoxia." (1995) J Clin Invest 95, 1798-1807.								
If you wish to add additional non-patent literature document citation information please click the Add button Add								
EXAMINER SIGNATURE								
Examiner	Signa	ure /Than	e Underdahl/			Date Considered	03/13/2009	
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.								

Application Number		10552194		
Filing Date		2006-10-12		
First Named Inventor Matth		ew Nugent		
Art Unit		1651		
Examiner Name Thane		E UNDERDAHL		
Attorney Docket Number		701586-053702		

<sup>&</sup>lt;sup>1</sup> See Kind Codes of USPTO Patent Documents at <u>www.USPTO.GOV</u> or MPEP 901.04. <sup>2</sup> Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>3</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>4</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>5</sup> Applicant is to place a check mark here if English language translation is attached.